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Vascular Pathology of Balloon-Expandable Flexible Coil Stents in Humans

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The morphologic changes in atherosclerotic coronary arteries and saphenous vein bypass grafts after placement of a balloon-expandable flexible coil stent (Cook) are described. In each case, the vessels were patent despite morphologic evidence of injury and dissection in the vessel wall. The stented region was reendothelialized and the tissue overlying the stent wires consisted primarily of smooth muscle cells. There was minimal inflammatory reaction to the stent wires.

These findings suggest that the balloon-expandable flexible coil stent can effectively maintain vessel patency even in the setting of postangioplasty lumen disruption. In addition, the vessels tolerate the metal prosthesis with little evidence of tissue inflammatory reaction.

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Intracoronary stent devices are now being investigated widely for the treatment of acute closure and restenosis in patients undergoing percutaneous transluminal coronary angioplasty for coronary artery disease. Despite the angiographic success rate of coronary angioplasty, acute vessel closure (seen in 3% to 5% of patients) and restenosis (seen in 25% to 40% of patients) continue to affect the clinical utility of this procedure (1,2). The pathophysiology of acute closure after angioplasty is a complex process that includes intimal arterial wall dissection, intramural plaque hemorrhage, thrombus formation, elastic recoil of the vessel and vascular spasm (3–7). Endovascular implants have been designed to reverse the untoward effects of angioplasty by acting as a scaffold to "tack-up" the intimal dissections, mechanically prevent elastic recoil and vascular spasm and possibly limit thrombus formation by increasing vessel blood flow (3–6,8–10). Clinical studies (11–15) have demonstrated that intravascular stents do improve stenosis geometry after angioplasty and have suggested that intracoronary stents may be effective in maintaining long-term vessel patency. Numerous experimental animal studies (14,16–19) have examined the short- and long-term morphologic effects of intravascular stents in coronary arteries; however, few studies (1,20) have evaluated these effects in human atherosclerotic vessels.

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Because of the relatively few patients who have undergone coronary stenting and the high success rate of this procedure, few pathologic specimens are available for evaluation. With the increasing use of intracoronary prosthetic devices, it is important that the vascular tissue reaction to these materials be evaluated in humans. We describe the morphologic characteristics of human coronary arteries and saphenous vein bypass grafts after placement of a balloon-expandable flexible coil stent (Cook) in four patients.

Methods

Study patients. A balloon-expandable flexible coil stent was placed in coronary arteries and saphenous vein bypass grafts in 179 patients from October 1989 through June 1991 at the University of Alabama at Birmingham. The procedures used and the clinical follow-up data of these patients have been described (16). From this group of patients, four specimens were available for morphologic examination. One patient died 18 h after an intracoronary stent was placed in the left main coronary artery and a second patient died 21 days after a stent was placed in the left anterior descending coronary artery. Autopsy was performed and tissues from these patients were available for examination. Saphenous vein bypass grafts from two patients who received a stent 19 and 24 weeks previously, respectively, became available for morphologic examination when repeat bypass surgery was performed.

Morphologic techniques. Tissue samples from these autopsy and biopsy specimens were fixed in 10% neutral buffered formalin. Vessels containing a stent were carefully dissected after fixation with use of a scalpel blade. The soft tissue was carefully cut and the stent wires were transected

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with fine wire cutters. The stent wires were then removed from the tissue specimen with fine forceps to minimize distortion of the neointima and vessel wall. Cross sections and longitudinal sections of the vessels were paraffin-embedded and 5-μm sections were stained with hematoxylin and eosin. Serial sections were also stained with aldehyde fuchsin Gomori's trichrome stain. Selected paraffin-embedded tissue sections were evaluated by immunohistochemistry, using the peroxidase-antiperoxidase technique as previously described (21,22). Antibodies to smooth muscle (alpha-actin, desmin, vimentin and factor VIII) were obtained from Dako. Selected formalin-fixed tissue specimens were transferred to 2% glutaraldehyde for 24 h and were then postfixed in buffered osmium tetroxide for 4 h, dehydrated and sputter-coated with gold for scanning electron microscopy. Samples were examined with a Philips 515 scanning electron microscope.

Results

Autopsy Results

Case 1. The first patient was an 80-year old woman with a long history of coronary artery disease and recurrent angina. She underwent saphenous vein-coronary artery bypass grafting 10 months before her last hospital admission. At her final admission, cardiac catheterization revealed occlusion of the bypass graft to the left anterior descending coronary artery and 95% stenosis of the ostium of the left main coronary artery. Angioplasty of the ostial lesion was performed, but the patient's condition deteriorated and she was returned to the coronary care unit receiving circulating assistance provided by an aortic balloon pump. Her condition continued to deteriorate and the next day a 20-mm long, 3.5-mm diameter stent was placed in the left main coronary artery. Despite this procedure, there was residual ostial stenosis, and the patient died 12 h after stent placement.

At autopsy, the aortic root contained extensive atherosclerosis with ulcerated plaques. These atherosclerotic lesions involved the ostia of the coronary arteries and the saphenous vein graft. The aorta surrounding the ostium of the left main coronary artery contained large atherosclerotic plaques that formed the ostial occlusion. Just distal to the ostium, the stented segment of the left main coronary artery was patent. There was histologic evidence of compression and dissection of the vessel wall in the proximal stented region of the left main coronary artery, but the vessel lumen was widely patent with no evidence of thrombus. There was significant coronary artery disease in the remainder of the coronary circulation and evidence of early myocardial infarction, with areas of contraction band formation in the anterior wall of the left ventricle.

Case 2. The second patient was a 71-year old man admitted for elective cardiac catheterization because of accelerating angina. Catheterization demonstrated 80% stenosis of the left anterior descending coronary artery (Fig. 1A), diffuse distal left circumflex disease, 90% stenosis of the second marginal branch and a dominant right coronary artery with diffuse lumen irregularities. Left ventricular function was normal. The patient later returned to the catheterization laboratory for coronary angioplasty, at which time a 20-mm long, 3-mm diameter ACS Pinkerton balloon was used to dilate the left anterior descending coronary artery lesion (Fig. 1B). Five minutes after the final balloon inflation, there was a significant reduction in the angioplasty gain, with sluggish flow and threatened vessel closure. Chest pain with electrocardiographic (ECG) changes and mild hypotension (systolic pressure 90 mm Hg) developed. Intracoronary nitroglycerin was given, but no angiographic change was noted. A 20-mm long, 3-mm diameter balloon-expandable flexible coil stent was inserted with a single inflation of 6 atm for 60 s (Fig. 1C). Angiographic results were good (<10% residual stenosis) (Fig. 1D), the patient's blood pressure increased and the chest pain and ECG changes resolved. He received a total of 20,000 U of heparin.

One hour after stent placement, the chest pain recurred and the patient became hypotensive. He was immediately returned to the catheterization laboratory where an intraaortic balloon pump was placed and the patient required insertion of an endotracheal tube, after which aspiration occurred. A repeat angiogram demonstrated that the stented vessel was widely patent. The sudden onset of angina after stent placement was thought to be caused by vascular spasm in a segment of artery adjacent to the stented region, but this possibility could not be documented angiographically. The condition of the patient was stabilized and gradually improved over the course of the next week, with removal of the intraaortic balloon pump and discontinuation of pressor support. The normal poststenting regimen of aspirin, dipyridamole, a calcium channel blocking agent and warfarin (Coumadin) was administered. The patient developed bilateral pneumonia, probably secondary to aspiration, became febrile and received aggressive antibiotic coverage. His condition gradually declined and approximately 2 weeks after stent placement, he developed ECG changes consistent with lateral wall infarction. His condition continued to deteriorate and he died 3 weeks after stent placement.

The autopsy was limited to the heart and lungs. The heart was extirpated, the aorta cannulated and the heart perfused with saline solution followed by 10% neutral buffered formalin. Pathologic evaluation of the lungs revealed bilateral pleural effusions, bilateral bronchopneumonia with positive cultures of *Staphylococcus aureus* and *Enterobacter* organisms and multiple abscesses in the right upper lobe. The heart was moderately enlarged (450 g). Evaluation of the coronary arteries revealed stenoses consistent with the catheterization findings. The second marginal artery was completely occluded by thrombotic material. Histologically, this marginal artery had multiple small vascular channels, consistent with the morphology of a recanalized thrombus. Within this region of recanalized thrombus, there was a new

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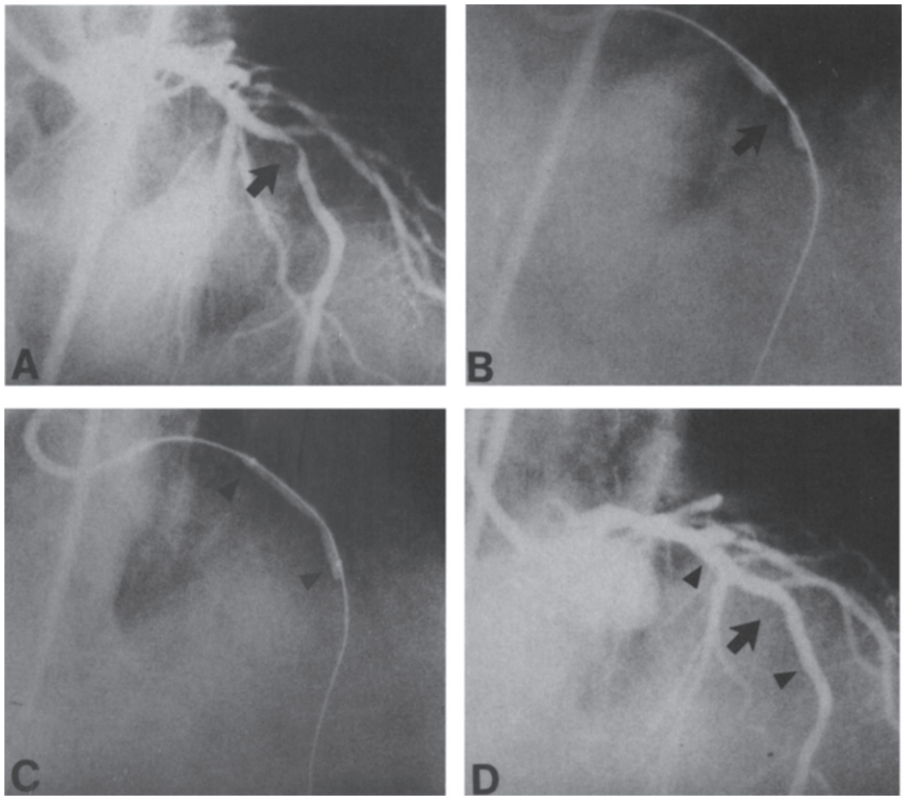

Figure 1. Case 2. Angiograms of the left anterior descending coronary artery. **A,** Before angioplasty. The **arrow** denotes the lesion. **B,** Balloon dilation with an ACS Pinkerton balloon. The **arrow** denotes the lesion. **C,** Placement of balloon-expandable flexible coil stent. **Arrowheads** mark the proximal and distal extent of the stent. **D,** After stenting. The **arrow** denotes the lesion and **arrowheads** mark the proximal and distal extent of the stent.

acute thrombotic occlusion. Distal to this artery, there was a large lateral wall infarct, which by histologic criteria was approximately 5 to 7 days old.

The left anterior descending coronary artery was isolated and the region containing the intracoronary stent identified (Fig. 2A). The vessel was widely patent and contained no thrombotic material. Sections of the left anterior descending coronary artery proximal to the stented region that had undergone balloon angioplasty demonstrated an intimal tear and a dissection flap (Fig. 2B). The proximal portion of the stented artery was sectioned transversely and the region of the stented segment containing the diagonal artery was sectioned longitudinally. On opening the vessel, no thrombotic material was present in the lumen. The stent wires could be visualized through a thin neointimal covering (Fig. 3). Scanning electron microscopy of this region demonstrated a thin neointimal covering over the stent wires (Fig. 4). The disruption of this neointima was due to postmortem autolysis and processing artifact. The stent wires were embedded in the wall of the artery and the neointima

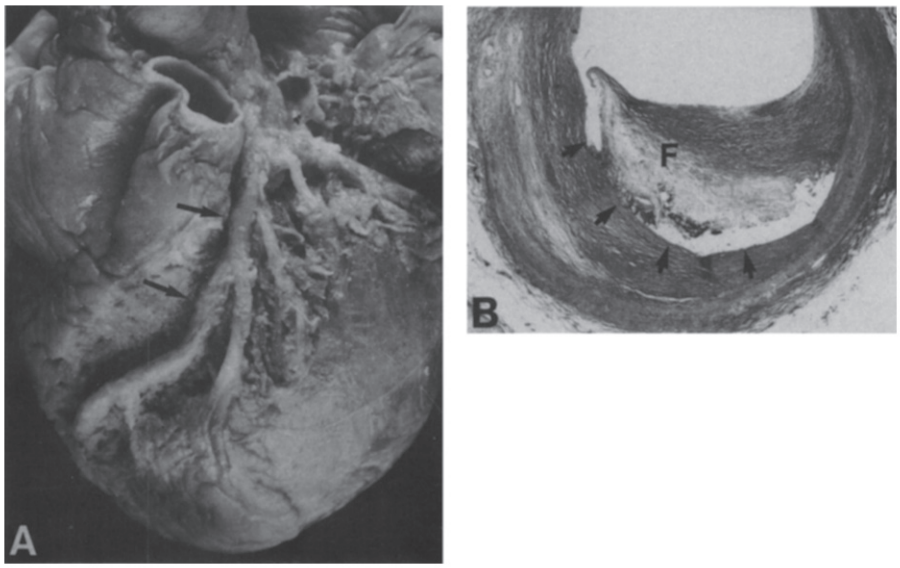

Figure 2. Case 2. **A,** Photograph of the anterior surface of the heart at autopsy. The epicardial fat has been dissected away to expose the coronary arteries. **Arrows** point to the proximal and distal extent of the stent in the left anterior descending coronary artery. **B,** Photomicrograph of a cross section of this artery proximal to the stent, within the region that underwent balloon angioplasty. There is an intimal dissection (**arrows**) with a dissection flap (F). Trichrome stain ×20, reduced by 30%.

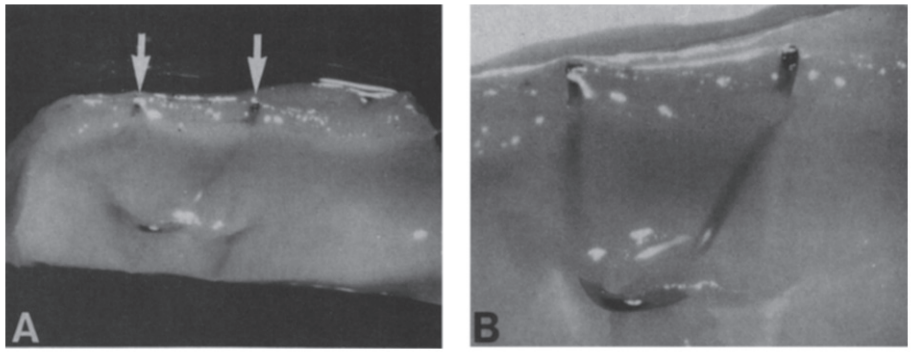

Figure 3. Case 2. Photographs of the lumen surface of the stented region of the left anterior descending coronary artery. **A,** The stent wires were cut with fine wire cutters and the cut ends of the wires can be seen embedded in the vessel wall (**arrows**). **B,** Higher power photograph demonstrating the smooth neointima covering the stent wire. The curved end of the stent wire tore through the neointima during postmortem dissection of the specimen.

covered by endothelial cells (Fig. 4, C and D). The endothelial cells were slightly rounded and raised, but the endothelial covering was complete on all sections examined.

Photomicrographs of histologic cross sections of the stented left anterior descending coronary artery just distal to the diagonal artery are shown in Figure 5. The low power photomicrograph (Fig. 5A) shows the hole left by the stent and the thin neointimal covering, which ranged from 30 to 50 μm in thickness. This photograph demonstrates how the stent wire acted as a scaffold, holding the intimal flap against the wall of the vessel. Note that the vessel is widely patent and no thrombotic material is present within the lumen. Figure 5B is a higher power photomicrograph demonstrating the dissection flap and the dissection plane, which is now partially healed. Figures 5C and 5D are photomicrographs of longitudinal sections of the stented left anterior descending coronary artery segment. Again, the dissection plane is visible as well as the indentations in the media where the stent wires held the dissection flap against the vessel wall. The neointimal tissue overlying the stent wire consists of spindle-shaped cells with eosinophilic interstitial tissue. These formalin-fixed paraffin-embedded slides were immunostained with smooth muscle alpha-actin, desmin, vimentin and factor VIII. The spindle-shaped cells in the neointima reacted positively with smooth muscle alpha-actin, vimentin and desmin antibody.

This morphology and the immunohistochemical staining characteristics are consistent with neointima containing

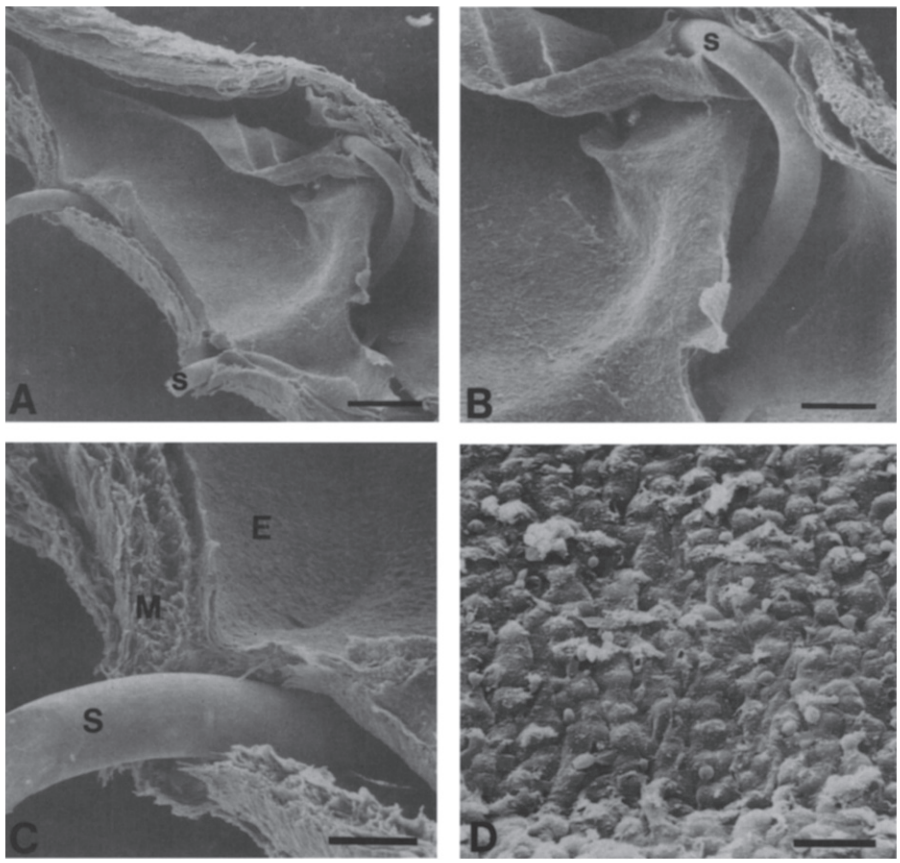

Figure 4. Case 2. Scanning electron micrographs of the lumen surface of the stented vessel. **A,** Low power view of the opened vessel showing the stent wires (s) covered by neointima. The neointima covering the stent wires has pulled away from the vessel wall during processing. **Bar** = 500 μm. **B,** A higher power micrograph showing the neointima covering the stent wire (s). **Bar** = 250 μm. **C,** The stent (S) is embedded into the media (M) of the vessel. The neointima is covering the stent wire and is covered by endothelial cells (E). **Bar** = 150 μm. **D,** Endothelial cells covering the neointima are slightly rounded and raised, but they form a contiguous endothelial covering within the vessel lumen of the stented region. **Bar** = 25 μm.

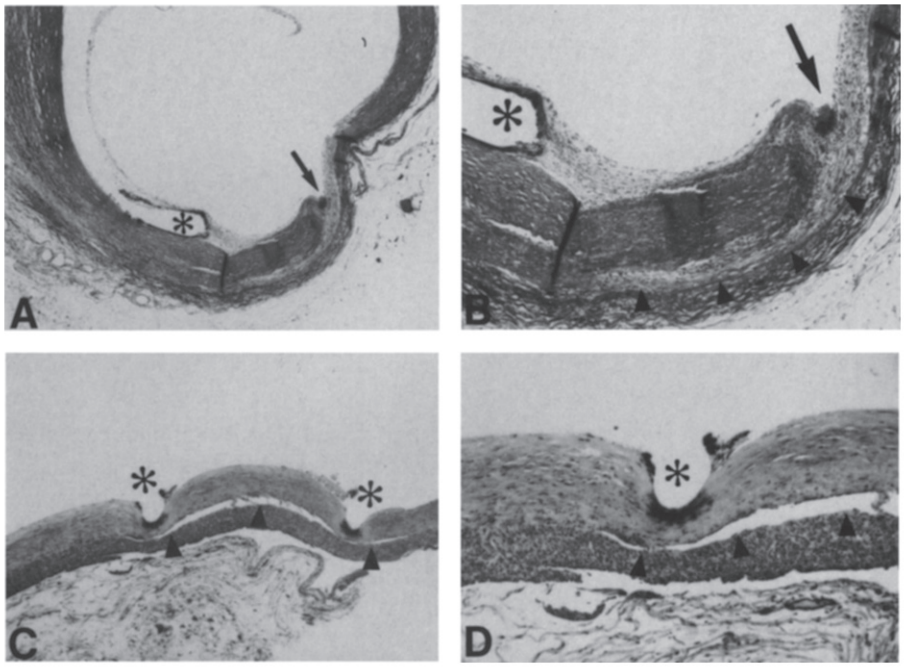

Figure 5. Case 2. Photomicrograph of trichrome-stained histologic section from the stented region of the left anterior descending coronary artery. **A,** The stent wire had been carefully removed before processing. The thin neointimal covering can be seen overlying the area where the stent wire has been removed (**asterisk**). The intimal flap (**arrow**) has been held against the vessel wall by the stent. ×20, reduced by 30%. **B,** The dissection plane of the intimal flap (**arrowheads**) is clearly visible; however, the stent (**asterisk**) has held the flap against the vessel wall and neointimal tissue has reattached the flap to the vessel wall (**arrow**). ×40, reduced by 30%. **C** and **D,** Longitudinal sections of the vessel demonstrate the indentations left by the stent wires (**asterisks**) and the dissection plane (**arrowheads**). The neointima was accidentally removed with the stent wires during preparation of the specimen for microscopy. ×60, reduced by 30%. **D,** The stent wire (**asterisk**) compressed the media and held this tissue against the vessel wall. ×80, reduced by 30%.

smooth muscle cells that are in the secretory phenotype. The cells lining the vessel lumen, including the neointimal area overlying the stent wires, reacted with factor VIII, a characteristic of endothelial cells. Serial sections throughout the stented region of the left anterior descending coronary artery demonstrated evidence of the angioplasty dissection and disruption of the media. There was only mild residual stenosis that did not exceed 20% to 30%.

Saphenous Vein Bypass Graft Biopsy Specimens

Case 3. The third patient was a 65-year old man with a history of previous saphenous vein coronary artery bypass grafting. He subsequently developed unstable angina and underwent catheterization at another hospital. Angioplasty of the bypass graft to the left anterior descending coronary artery was attempted, but residual stenosis remained. The patient was transferred to this institution, where angiography of the bypass graft demonstrated a 90% ostial lesion of the graft, 30% to 40% lesions in the midportion of the graft and 95% stenosis of the anastomotic site with the left anterior descending coronary artery (Fig. 6A). Angioplasty of the distal (anastomotic site) lesion was performed with a 20-mm long, 2-mm diameter ACS Pinkerton catheter for 285 s at 10 atm. A 20-mm long, 2.5-mm diameter Pinkerton catheter was exchanged, advanced to the distal lesion site and inflated to 10 atm for 220 s.

Stent placement. After these procedures, there was still a suboptimal angiographic result and at this point a 20-mm long, 2.5-mm diameter balloon-expandable flexible coil stent was deployed with use of a 220-s inflation at 7 atm (Fig. 6B and C). The proximal aspect of the stent was placed in the distal portion of the graft and the stent extended through the anastomotic site into the native left anterior descending coronary artery. The balloon catheter used to deploy the stent was then withdrawn to the ostial lesion (Fig. 7A) and two inflations were performed (8 atm for 60 s; 10 atm for 60 s). Because the angiographic results demonstrated a residual stenosis, a 20-mm long, 3.5-mm diameter balloon-expandable flexible coil stent was deployed at the ostial lesion with use of a 120-s inflation at 7 atm. The balloon catheter was deflated and withdrawn slightly and the ostial lesion including the stent was dilated again at 8 atm for 111 s (Fig. 7B). The angiographic results were deemed to be satisfactory with ≤30% residual stenosis in the ostial lesion, 20% to 30% stenosis in the anastomotic lesion and 30% to 40% stenosis in the midportion of the graft that was not dilated.

After stent placement, the patient did well and was free from angina for 19 weeks when chest pain again developed. Cardiac catheterization was performed at another institution where examination of the bypass graft demonstrated 95% stenosis of the lesion at the anastomotic site to the left anterior descending coronary artery (Fig. 6D) and 60% stenosis of the ostial lesion (Fig. 7C). The patient then underwent a repeat saphenous vein coronary artery bypass grafting procedure to the diagonal branch and the distal left anterior descending coronary artery. During the operation, the original saphenous vein graft to the left anterior descending coronary artery, which included the stents, was removed and saved for pathologic examination. During the surgical procedure, the wires from the proximal stent were partially removed from the vein graft and accurate orientation of the

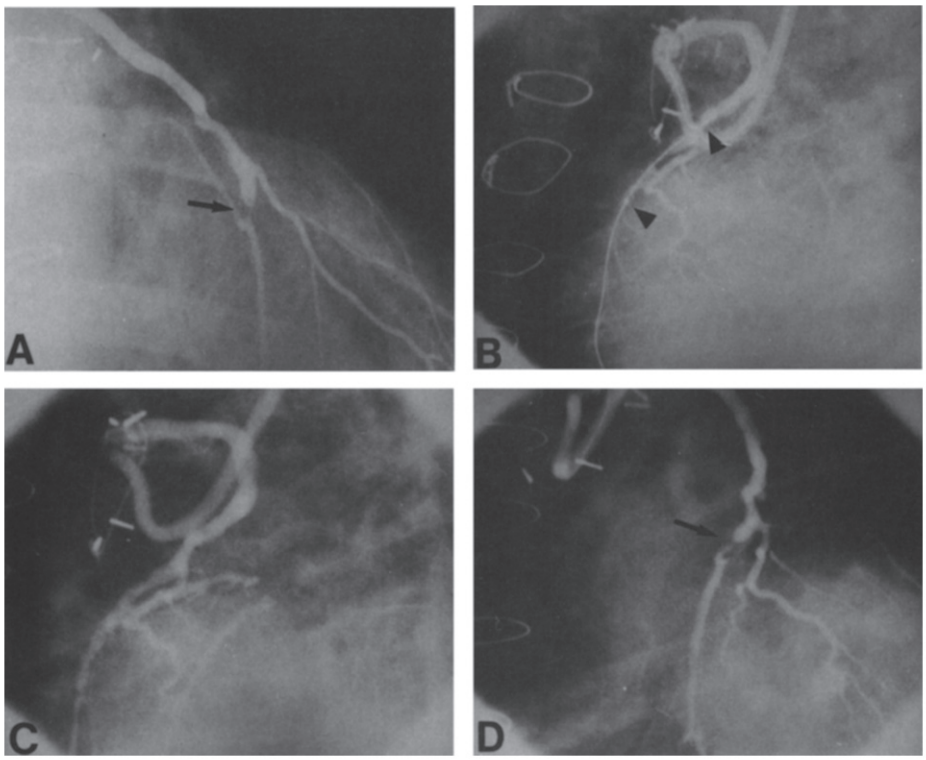

Figure 6. Case 3. Angiograms demonstrating the stenoses in the saphenous vein graft to the first diagonal branch and the distal left anterior descending coronary artery. **A,** Tight stenosis at the distal anastomotic site (**arrow**). **B,** Stent placement after attempted angioplasty. **Arrowheads** denote proximal and distal extent of the stent. **C,** Angiographic results after stenting. **D,** Restenosis of distal anastomotic site (**arrow**) to the left anterior descending coronary artery 19 weeks after stent placement.

tissue specimens was difficult. Also, the distal portion of the vein graft and the left anterior descending coronary artery were opened at operation and the stent wire was removed. This portion of the specimen was not saved intact.

Pathologic examination. The sections of saphenous vein graft submitted for pathologic examination were patent; however, the vessel walls were markedly thickened by fibrous connective tissue. The portion of the graft that had

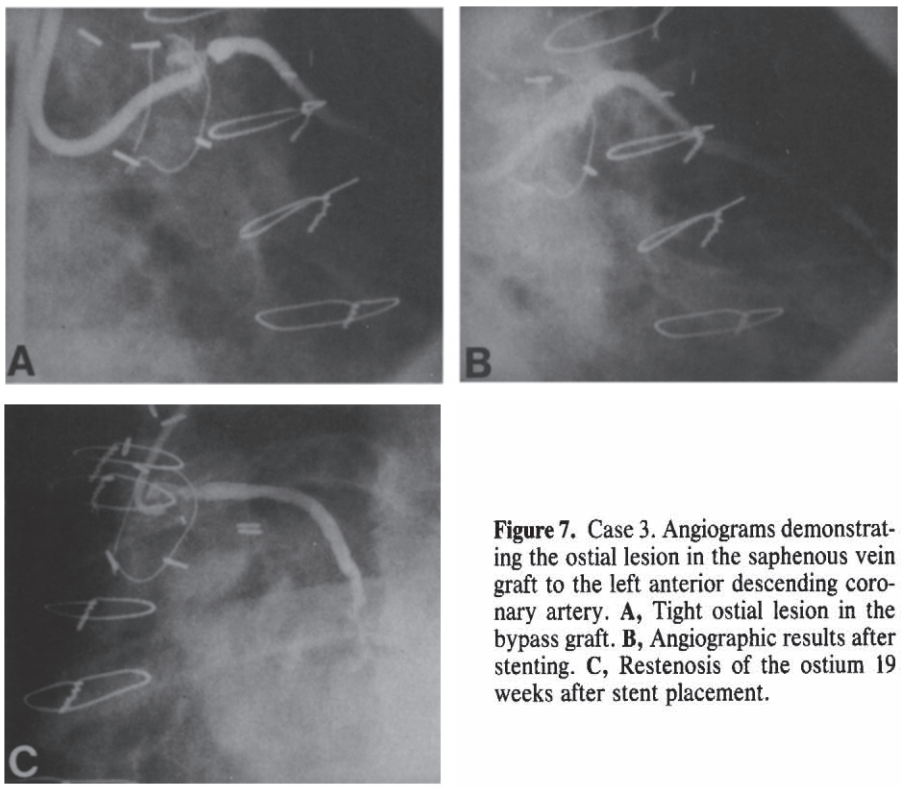

Figure 7. Case 3. Angiograms demonstrating the ostial lesion in the saphenous vein graft to the left anterior descending coronary artery. **A,** Tight ostial lesion in the bypass graft. **B,** Angiographic results after stenting. **C,** Restenosis of the ostium 19 weeks after stent placement.

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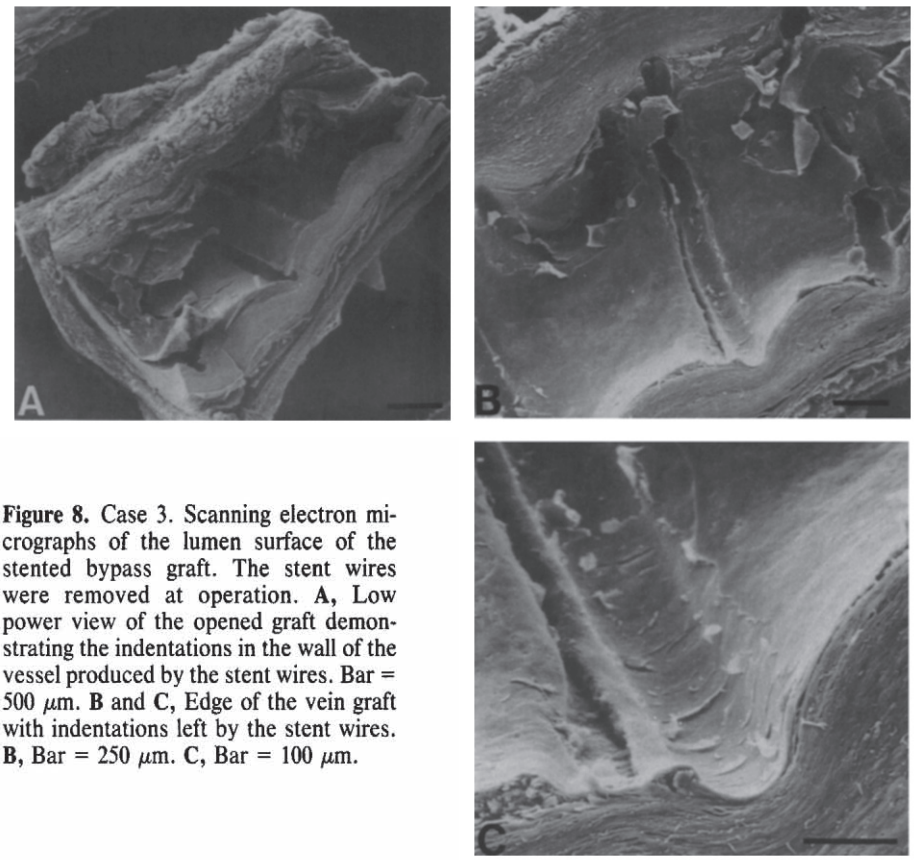
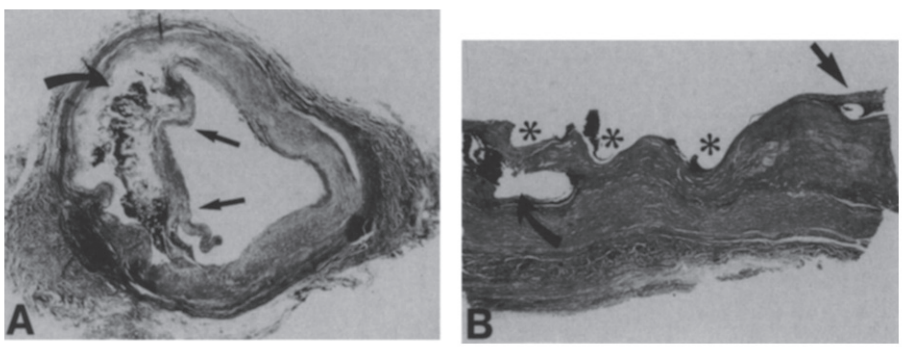


Figure 8. Case 3. Scanning electron micrographs of the lumen surface of the stented bypass graft. The stent wires were removed at operation. **A,** Low power view of the opened graft demonstrating the indentations in the wall of the vessel produced by the stent wires. Bar = 500 μm. **B** and **C,** Edge of the vein graft with indentations left by the stent wires. **B,** Bar = 250 μm. **C,** Bar = 100 μm.

Figure 9. Case 3. **A,** Photomicrograph of a cross section of saphenous vein graft just distal to the stented proximal portion of the graft. The vessel wall is thickened and there is an eccentric atheromatous lesion (**curved arrow**) with a fibrous cap (**small arrows**). This lesion contains fresh hemorrhage. Hematoxylin-eosin stain ×15, reduced by 30%. **B,** Longitudinal section of stented portion of the vein graft just proximal to the segment shown in **A**. The atheromatous lesion (**curved arrow**) with the fibrous cap can be seen. The indentations left by the stent wires (**asterisks**) are visible on the lumen surface of the vessel. One of these stent wires (**left side of figure**) compresses the fibrous cap overlying the atheromatous lesion. The neointima was artifactually removed over most of this specimen during processing of the tissue samples, except in the area shown at the **far right** (**arrow**). In this region, the hole left by the stent wire is visible and the neointima has grown over the wire (**arrow**). Hematoxylin-eosin stain ×30, reduced by 30%.

contained the distal portion of the stent that was placed in the ostial lesion was examined by scanning electron microscopy (Fig. 8). Although the stent wires were removed at operation, the indentations where the stent wires were embedded in the wall of the vessel are still apparent. The thickened vessel wall is clearly seen in these specimens. Light microscopic evaluation of these specimens demonstrates the thickened intima and a large eccentric atherosclerotic plaque in the proximal segment of the vein graft (Fig. 9A). The fibrous cap overlying this atheromatous lesion is clearly visible. Just proximal to this section, the vein graft was cut longitudinally (Fig. 9B). This section again demonstrates the marked thickening of the vessel wall. The indentations produced by the stent wires are visible and one of these stent wire indentations (left side of Fig. 9B) is com-



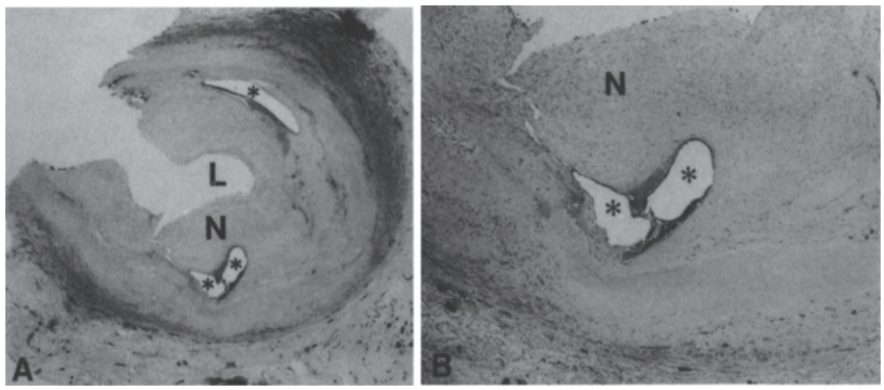


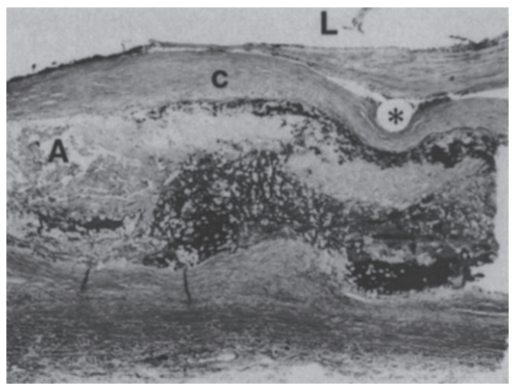
Figure 10. Case 4. **A,** Photomicrograph of a cross section of the saphenous vein graft in this patient showing the holes left after stent wire removal (**asterisks**) and the exuberant neointimal tissue (N) overlying the stent. ×10, reduced by 30%. **B,** High power photomicrograph of the saphenous vein graft wall showing the holes left by the stent wires (**asterisks**) and the neointimal covering (N). ×30, reduced by 30%. L = vessel lumen.

pressing the fibrous cap overlying the atheromatous lesions seen in cross section in Figure 9A. Another stent wire indentation (far right of Fig. 9B) still has the neointimal covering over the hole left by the stent wire. The neointimal covering ranged from 100 to 150 μm in thickness and was composed of fusiform-shaped cells that stained positively with smooth muscle alpha-actin antibody, which is characteristic of smooth muscle cells. These smooth muscle cells have very little extracellular matrix and have a more mature (contractile type) morphology as compared with the secretory phenotype cells seen in the previous case where the stent had been implanted for only 3 weeks. There are also occasional round cells (lymphocytes and macrophages) within the neointima covering the stent wire. The cells are diffusely distributed within the neointima and are not associated with or concentrated around the stent wire. These findings suggest that this inflammatory reaction is a general reaction within the vessel wall and is not associated with a rejection reaction to the wire. There was no evidence of inflammatory reaction associated with the stent wires in these specimens.

Case 4. The fourth patient was a 50-year old man with severe coronary artery disease who had saphenous vein bypass grafting performed at 40 years of age. Ten years later, he developed a non-Q wave myocardial infarction and cardiac catheterization revealed occlusion of the bypass graft to the right coronary artery and a 90% stenotic lesion in the midportion of the bypass graft to the left circumflex coronary artery. Successful angioplasty with adjunctive use of the excimer laser was subsequently performed. Two months later, the patient again experienced angina and catheterization demonstrated recurrent graft stenosis. A 20-mm long, 3-mm diameter balloon-expandable flexible coil stent was inserted at the lesion site, leaving a residual stenosis of 15% to 20%. Five months later, the patient again developed angina and angioplasty was performed inside the stent. A 20-mm long, 1.5-mm diameter ACS Alpha angioplasty balloon was used to predilate the lesion and a 20-mm long, 3.5-mm diameter ACS RX perfusion balloon was advanced to the lesion and inflated to 6 atm for 14 min. Repeat angiograms demonstrated excellent resolution of the stenosis. One month later, angina again developed and at this time, internal mammary artery bypass grafting was performed. During the operation, the saphenous vein bypass graft containing the stent was retrieved and was available for morphologic examination.

Pathologic examination. The saphenous vein bypass graft was markedly thickened and contains extensive neointimal proliferation (Fig. 10A and B). The neointima ranged from 250 to 500 μm in thickness. This neointimal tissue clearly obstructed the lumen of the saphenous vein graft. The vessel wall contained an area of atheromatous material with an overlying fibrous cap (Fig. 11). In Figure 11, the indentations produced by the stent wires can be seen with a neointimal covering overlying the stents. The stent wires compress the fibrous cap overlying the atheromatous lesion. The neointima contains spindle-shaped smooth muscle cells similar to those seen 19 weeks after stenting in Case 3. The neointima also contained some lymphocytic infiltration. There was minimal inflammation associated with the stent wires in the vessel wall.

Figure 11. Case 4. Longitudinal section of the saphenous vein graft shown in Figure 10. The atheromatous lesion is within the wall of the vessel (A) that is covered by a fibrous connective tissue cap (c). The hole left by the stent wire (**asterisk**) indents the fibrous cap and holds it against the atheromatous plaque. The neointimal tissue is seen overlying the stent and consists of spindle-shaped smooth muscle cells with a mild lymphocytic infiltrate. ×30, reduced by 30%. L = vessel lumen.



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Discussion

The balloon-expandable flexible coil stent has been extensively evaluated in animal models, but the morphologic changes in human vessels have not been reported previously. The cases presented in this report demonstrate that the balloon-expandable stent is effective in maintaining vessel geometry even in the setting of intimal dissections. In these cases, there was no evidence of thrombus formation related to the stent wires and in as little time as 3 weeks, the stent region had reendothelialized. In addition, there was no morphologic evidence of untoward tissue reaction to the stent wires in these vessels.

Reported experience with intracoronary stents. The balloon-expandable flexible coil stent was designed to eliminate the problems of elastic recoil after angioplasty and to improve vessel lumen morphologic deterioration due to dissections and intimal disruption during angioplasty. After balloon expansion, the stent coils are embedded into the surface of the vessel lumen, producing a radial scaffolding for the lumen. This improvement in postangioplasty vessel geometry is intended to help prevent acute closure. Angiographically visible intimal tears or dissections are seen in approximately 20% of patients after angioplasty (3,6,7). The pathophysiology of postangioplasty vascular occlusion is multifactorial and includes the disruption of the arterial wall, hemorrhage into atheromatous plaques, thrombus formation, elastic recoil of the vessel wall and vascular spasm (3,7). Placement of an endovascular prosthesis immediately after angioplasty is intended to prevent these untoward events. The intracoronary stent is designed to "tack-up" the intimal dissection, mechanically prevent elastic recoil and vascular spasm and prevent thrombus formation by increasing blood flow (2,4,5,14). Angiographic results in patients with an intracoronary stent have demonstrated significant improvement of vessel geometry and blood flow in the stented region (11–14), thus demonstrating the effectiveness of this technique in maintaining vessel patency. The intracoronary stent was initially used as a bridge to bypass surgery in patients with acute vessel closure (14), but more recently, the stent has been used as definitive therapy to prevent acute closure (1,2,14,16,20). The patients described in this report were in this latter group. The clinical procedures and follow-up data for these patients have been described previously (16).

Morphologic changes seen in stented coronary arteries and saphenous vein bypass grafts from patients with atherosclerotic coronary artery disease. The four specimens that we describe are the only specimens that have become available from our series of patients undergoing coronary stenting. A previous morphologic study (1) of stents in humans utilized stents that are much more rigid and cover more surface area than the flexible coil stent. In that study (1), the restenotic tissue consisted of proliferating smooth muscle cells that grew over the stent wires and was reendothelialized. This morphology is similar to that observed in our four cases. The coronary artery that was stented 3 weeks before examination demonstrated loose spindle-shaped smooth muscle cells with abundant eosinophilic interstitial tissue growing over the stent wires luminally. This morphology is consistent with smooth muscle cells that have changed to a secretory phenotype. In the saphenous vein grafts that had been in place for 19 and 24 weeks, respectively, the tissue overlying the stent wires consisted of smooth muscle cells with abundant eosinophilic cytoplasm and minimal interstitial tissue. The smooth muscle cells that migrated into the intima and covered the stent wires would be expected to have a secretory phenotype; however, after 19 to 24 weeks, the smooth muscle cells have reverted to the contractile phenotype. This change to the contractile phenotype has previously been observed in rabbit carotid arteries subjected to balloon injury (23).

In the two saphenous vein bypass cases reported here, severe restenosis occurred in the stented region of the vessel. In both cases, the patients had a history of restenosis before stent placement. Although the poststenting angiographic results were deemed to be satisfactory in both cases, the progression of exuberant neointimal proliferation was not abated. This neointimal tissue growth occurred on the luminal aspect of the stent wires and resulted in significant stenosis of the affected vessel. Thus, stenting with adequate restoration of vessel geometry did not prevent restenosis in these two cases in which restenosis had already been a problem.

Conclusions. This report describes the morphologic changes noted in atherosclerotic human vessels after placement of a balloon-expandable flexible coil stent. In these cases, the vessels were patent despite morphologic evidence of injury and dissection of the vessel wall. The stented region was reendothelialized and the tissue overlying the stent wires consisted primarily of smooth muscle cells. There was minimal inflammatory reaction to the stent wires. Thus, these initial findings suggest that a balloon-expandable flexible coil stent can effectively maintain vessel patency even in the setting of postangioplasty lumen disruption. In addition, the vessels tolerate the metal prosthesis with little evidence of tissue inflammatory reaction.

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References

1. Schatz RA, Baim DS, Leon M, et al. Clinical experience with the Palmaz-Schatz coronary stent: initial results of a multicenter study. Circulation 1991;83:148–61.
2. Ellis SG, Topol EJ. Intracoronary stents: will they fulfill their promise as an adjunct to angioplasty? J Am Coll Cardiol 1989;13:1425–30.
3. Murphy JG, Garratt KN, Schwartz RS, Holmes DR Jr. Intracoronary stenting: bailout or bypass? Cathet Cardiovasc Diagn 1990;21:260–2.
4. Lembo NJ, Roubin GS. Intravascular stents. Cardiol Clin 1989;7:877–94.

5. Schatz RA. A view of vascular stents. Circulation 1989;79:445–57.
6. Black AJR, Namay DL, Niederman AL, et al. Tear or dissection after coronary angioplasty: morphologic correlates of an ischemic complication. Circulation 1989;79:1035–42.
7. Waller BF. Crackers, breakers, stretchers, drillers, scrapers, shavers, burners, welders and melters: the future treatment of atherosclerotic coronary artery disease? A clinico-morphologic assessment. J Am Coll Cardiol 1989;13:969–87.
8. Sigwart U, Urban P, Golf S, et al. Emergency coronary artery stenting for acute occlusion after coronary balloon angioplasty. Circulation 1988;78: 1121–7.
9. Strauss BH, Leborgne O, De Scheerder IK, Serruys PW. Implantation of an endoluminal prosthesis at the distal anastomosis of a bypass graft for abrupt closure following balloon angioplasty. Cathet Cardiovasc Diagn 1990;21:271–4.
10. Mehl JK, Schieman G, Dittrich H, Buchbinder M. Emergent saphenous vein graft stenting for acute occlusion during percutaneous transluminal coronary angioplasty. Cathet Cardiovasc Diagn 1990;21:266–70.
11. Serruys PW, Juilliere Y, Bertrand ME, Puel J, Rickards AF, Sigwart U. Additional improvement of stenosis geometry in human coronary arteries by stenting after balloon dilatation. Am J Cardiol 1988;61:71G–6G.
12. Levine MD, Leonard BM, Burke JA, et al. Clinical and angiographic results of balloon-expandable intracoronary stents in right coronary artery stenoses. J Am Coll Cardiol 1990;16:332–9.
13. Haude M, Erbel R, Straub U, Dietz U, Schatz R, Meyer J. Coronary stent implantation in acute vessel closure 48 hours after an unsatisfactory coronary angioplasty. Cathet Cardiovasc Diagn 1990;21:263–5.
14. Roubin GS, Robinson KS. The Gianturco-Roubin stent. In: Topol EJ, ed. Textbook of Interventional Cardiology. Philadelphia: WB Saunders, 1990:633–46.
15. Haude M, Erbel R, Straub U, Dietz U, Schatz R, Meyer J. Results of intracoronary stents for management of coronary dissection after balloon angioplasty. Am J Cardiol 1991;67:691–6.
16. Roubin GS, Cannon AD, Dean LS, et al. Intra-coronary stenting for acute and threatened closure complicating percutaneous transluminal coronary angioplasty. Circulation 1991 (in press).
17. Roubin GS, Robinson KA, King SB III, et al. Early and late results of intracoronary arterial stenting after coronary angioplasty in dogs. Circulation 1987;76:891–7.
18. Schwartz RS, Murphy JG, Edwards WD, Camrud AR, Vlietstra RE, Holmes DR. Restenosis after balloon angioplasty: a practical proliferative model in porcine coronary arteries. Circulation 1990;82:2190–200.
19. Rodgers GP, Minor ST, Robinson K, et al. Adjuvant therapy for intracoronary stents: investigations in atherosclerotic swine. Circulation 1990; 82:560–9.
20. Serruys PW, Strauss BH, Beatt KJ, et al. Angiographic follow-up after placement of a self-expanding coronary artery stent. N Engl J Med 1991;324:13–7.
21. Anderson PG, Capen CC. Undifferentiated spindle cell carcinoma of the thyroid in a dog. Vet Pathol 1986;23:203–4.
22. Burke AP, Anderson PG, Virmani R, James TN, Herrera GA, Ceballos R. Tumor of the atrioventricular nodal region. Arch Pathol Lab Med 1990;114:1057–62.
23. Manderson JA, Mosse PRL, Safstrom JA, Young SB, Campbell GR. Balloon catheter injury to rabbit carotid artery: I. Changes in smooth muscle phenotype. Arteriosclerosis 1989;9:289–98.